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Case Report

Pathology Section

Pseudoactinomycotic Radiate Granules (PAMRAGs)- An Unusual Differential Diagnosis for Ovarian Neoplasm; A Diagnostic Dilemma

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ABSTRACT

Pseudoactinomycotic radiate granules (PAMRAGs) are rarely detected lesions in ovary. Endometrium is the usual site and a detailed search of literature yielded only two cases in the ovary. PAMRAGs must be differentiated from actinomycotic granules which are also strongly associated with the use of intrauterine contraceptive devices (IUCDs). In cases of suppurative oophoritis due to actinomycosis, a proper diagnosis and culture confirmation is mandatory to avoid further complications. This case is reported due to its rarity, unusual clinical presentation and to highlight the importance of special stains in cases of tuboovarian abscess, where PAMRAGs may cause diagnostic dilemma.

Our patient was a 50 yr old female admitted with clinical diagnosis of malignant ovarian tumour. After preoperative work up, panhysterectomy, infracolic omentectomy and excision biopsy of the right inguinal lymph node were done. Peroperatively the right ovary was enlarged and adherent to the fallopian tube and pelvic wall. Gross examination revealed a right tuboovarian mass with yellowish areas of necrosis and fibrosis. Histology showed a suppurative granulomatous lesion with spherical granules having club like peripheral projections. A panel of special stains (GMS, GRAMs and AFB) done were negative. Thus, we ruled out actinomycosis and gave a diagnosis of PAMRAG.

Keywords: Endometrium, Oophoritis, Tubo ovarian mass

CASE REPORT

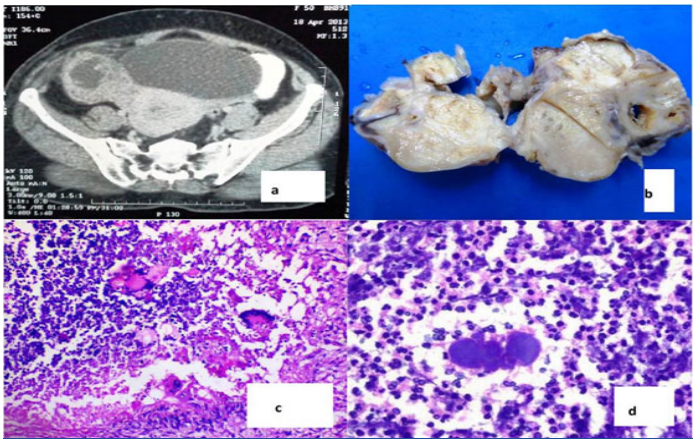
A 50-year-old lady, evaluated for lower abdominal pain was referred to our institution with a provisional diagnosis of ovarian tumour. She gave a history of vague abdominal pain for the last two years which aggravated since six months. Her cycles were irregular with two episodes of excessive bleeding. Fine needle aspiration cytology done from the enlarged right inguinal lymph node five months back showed suppurative necrosis with attempted granuloma formation. Fractional curettage done five months back showed disordered proliferative endometrium. There was no history of IUCD usage or MTP. No history of tuberculosis, pelvic inflammatory disease (PID) or any other significant illness in the past. She is a housewife with four children. On examination pallor was present. Right inguinal node was enlarged 2 x 1.5 cms. Per vaginal examination showed a bulky anteverted uterus with restricted mobility and a vague mass in the right adnexa.

Blood investigations showed Hb value of 8.3gm/dl and ESR -68mm/1ST hr. Cancer Antigen 125 and CEA were within normal range. Serial sonographic studies and CT scan revealed a heterogenous mass lesion in the right adnexa, measuring 7 x 5 cms which was adherent to the uterus, suggesting ovarian neoplasm [Table/Fig-1a]. Based on radiological studies a staging laparotomy along with biopsy of the enlarged right inguinal node was done. Per operatively there was a mass in the right adnexa and pus was found on releasing the adhesions. Pus was pale yellow and routine aerobic culture and sensitivity and AFB studies were found to be negative.

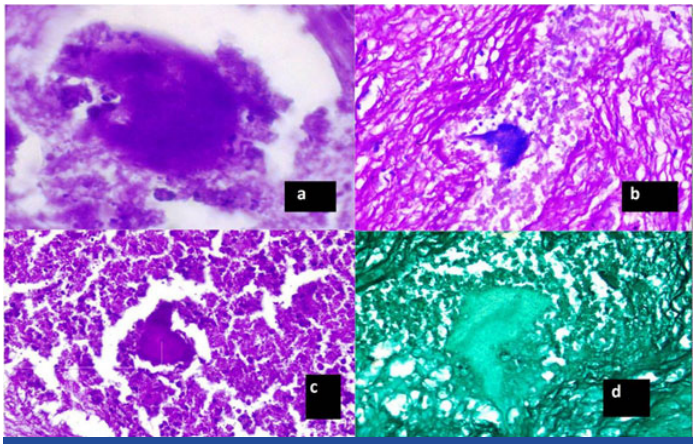
The gross specimen showed a right tubo ovarian mass measuring 6.5 x 5.5 x 2.5 cms and cut section showed solid grey white and yellowish areas [Table/Fig-1b]. But the uterus, left ovary and tube did not show any significant pathology. Initial histological evaluation revealed a suppurative granulomatous reaction with suspicious basophilic organisms [Table/Fig-1c,1d]. There was no evidence of malignancy as suspected clinically or radiologically. Multiple sections studied showed basophilic spherical granules and strips with broad peripheral clubs but no dense core [Table/Fig 1d,2a]. Considering the possibility of actinomycosis, a battery of special stains were done. The granules gave a non specific reaction with grams stain and negative reaction with modified AFB and GMS [Table/Fig2b-d]. Sections from inguinal node showed giant cell reaction only. Thus a diagnosis of PAMRAG was made.

DISCUSSION

PAMRAGs were first described by O'Brien et al., in 1981, in his study on endometrial curettings examined during IUCD removal [1]. They occur in the female genital tract, most commonly in the endometrium [1,2]. They are comparatively commoner than true actinomycotic infections in patients using IUCDs [1]. However occurrence in



[Table/Fig-1a-d]: (a) CT scan showing tuboovarian mass (b) gross photograph showing cut section of tuboovarian mass (c) photomicrograph showing suppurative granulomatous reaction,100 X (d) photomicrograph showing spherical basophilic granules with club like peripheral projections and surrounding neutrophilic infiltrate, 200 X



[Table/Fig-2a-d]: (a) Photomicrograph showing basophilic granules with neutrophilic infiltrate ,H&E 400X (b) photomicrograph showing non specific reaction with Grams stain.,100X (c) photomicrograph showing negative reaction on modified AFB stain,200X (d) photomicrograph showing negative reaction on GMS stain,200 X

extrauterine sites like ovaries are very rare and a thorough search of literature yielded only two cases. Otherwise known as pseudosulfur granules or radiate pseudocolonies, they are non-pathogenic and must be differentiated from true actinomycotic granules. They can masquerade as ovarian neoplasms when presenting as mass lesions in middle aged and elderly females. So, surgical intervention becomes mandatory in such cases. It is important to distinguish between these, since actinomycosis require antibiotic treatment while PAMRAG is non-infectious and does not require any specific treatment [3,4]. Reported cases of PAMRAGs in ovary are very few and this is the first reported case with a clinical and radiological impression of a malignant ovarian tumour.

Since initial reports of PAMRAGs were found in IUCD users, they were thought to be dissociated IUCD fragments. However this hypothesis was revised after identification of similar cases in patients without IUCDs. Moreover analysis by transmission electron microscopy did not demonstrate any IUCD fragments [3]. Further studies suggested that induction of increased lysosomal activity by exogenous factors may trigger formation of a nidus and ultimately result in the formation of PAMRAGs [5]. This trigger can include surface material from IUCD device, host polypeptides or even inspissated mucous of endocervical glands [5]. Some authors have likened PAMRAGs to Splendore Hoeppli (SH) phenomenon which is the in vivo formation of intensely eosinophilic material (radiate, star like, asteroid or club shaped configuration) around microorganisms or biologically inert substances [2,6]. But detailed immunohistochemical analysis showed absence of immunoglobulin, fibrin and complement, leading to the conclusion that PAMRAGs represent a non specific host leucocyte response to foreign body, parasites or bacteria [7]. Since there is a difference of opinion regarding the actual content of PAMRAGs, it may be suggested that the composition may vary in different cases [7]. Appearance of PAMRAGs can be quite confusing on routine histopathology (H & E stain) since they closely mimic actinomycotic granules. There are certain features which aid in differentiating them. PAMRAGs are seen as thick irregular club like peripheral projections without a central dense core. They may be spherical or appear as strips and are refractile but non birefrengent with polarized light. Surrounding neutrophilic reaction may be present. Actinomycotic granules are non refractile with thin basophilic radiating filaments and a central dense eosinophilic core. The recommended panel of special stains are Gomorri methenamine silver, Brown & Brenn tissue grams stain and modified AFB stain. All these stains were done in our case, and we got negative reaction with GMS and modified AFB and a non specific reaction with grams stain. Thus we excluded actinomycosis (gram positive) and nocardia (modified AFB positive) and arrived at a diagnosis of PAMRAG .

Due to the varied aetiology of tuboovarian masses, a proper work up is mandatory to delineate the underlying cause. This is of utmost importance when the clinical and sonological findings suggest neoplastic cause, as in our case. Though we excluded neoplastic aetiology after the initial histopathology evaluation, the exact cause was confirmed only after doing an array of special stains. Pathologists should be familiar with the existence and diagnostic criteria of PAMRAGs to avoid an erroneous diagnosis of actinomycosis since the management differs [7]. A proper antibiotic coverage is essential in actinomycosis, were as PAMRAGs do not contain microorganisms and are considered to be nonpathogenic. Since coexistence of PAMRAGs and actinomycosis have been reported, it is important that a detailed microscopic examination is done to exclude actinomycosis [2,8].This case highlights the importance of histopathological evaluation and judicious use of special stains.

CONCLUSION

There are multiple causes for tuboovarian masses, both neoplastic and non neoplastic. Hence a proper clinicopathological correlation and detailed workup is necessary to find out the underlying cause. Pathologists should be aware of this rare entity due to the superficial resemblance to actinomycosis and the varied treatment options.

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